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# COVID-Associated Exacerbation of Acute Psychosis in a Patient With Schizoaffective Disorder

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**T**he case presented here, to the best of our knowledge, represents a first in published literature, in which a patient with preexisting schizoaffective disorder experienced an acute worsening of psychosis temporally related to coronavirus disease 2019 (COVID-19) infection.

## Case Report

Mr A, a 36-year-old White man with a history of schizoaffective disorder (bipolar type), was admitted to the psychiatric hospital in August 2021 from a residential facility due to exacerbation of psychosis and mania in the setting of medication nonadherence. His symptoms had previously stabilized on clozapine 400 mg by mouth at night and haloperidol 10 mg by mouth at night. During hospitalization, haloperidol was titrated to 20 mg by mouth daily and 10 mg at night, but he declined to take clozapine due to the delusional belief that blood draws would kill him. While he continued experiencing auditory hallucinations and delusional ideation (eg, that he is an Italian vampire whose blood will not regenerate), he remained in good behavioral control, requiring no emergency involuntary procedures and typically scoring “small risk” (0) and always “moderate risk” or less ( $\leq 2$ ) on the twice-daily Brøset Violence Checklist<sup>1</sup> from September 24 to December 8, 2021. This lack of violence was consistent with his 15-year history since diagnosis of schizoaffective disorder.

On December 6, he received the first dose of the Janssen COVID-19 vaccine and, coincidentally, also tested positive for COVID-19 and was transferred to the COVID-19 unit.

COVID-19 symptoms were mild and included cough, myalgias, and fevers/chills. He refused vitals. These symptoms peaked on December 9. On December 9, his behavior acutely changed. Without provocation, he threw objects at staff and assaulted staff, requiring manual, mechanical, and pharmacologic restraints. Shortly after being released from restraints, he assaulted a staff member by chokehold, again requiring restraints. That night, he received a total of haloperidol 30 mg, diphenhydramine 100 mg, and lorazepam 4 mg by mouth. His escalated behavior continued the next day, during which he assaulted staff on 3 different occasions, including punching a staff member in the head with force, biting and breaking a staff member’s finger, and spraining another staff member’s wrist. His mental status examination showed intense eye contact, poverty of speech, thought blocking, and command auditory hallucinations telling him that he needed to hurt others to be calm and on the path of God.

In addition to his scheduled haloperidol 20 mg daily, over the course of 9 hours, the patient required high doses of emergency antipsychotics, including olanzapine 25 mg, chlorpromazine 300 mg, lorazepam 6 mg, and diphenhydramine 50 mg by mouth. By night, he engaged in a cooperative discussion about safety and was released from 4-point restraints. He demonstrated a marked improvement in psychotic symptoms and behaviors over the next week while starting clozapine titration. His COVID-19 symptoms resolved by December 13.

## Discussion

Evidence that infection may be an incipient factor in acute and chronic psychosis dates to when Menninger<sup>2</sup> published on 100 cases of psychosis and other neuropsychiatric sequelae during the 1918 influenza pandemic. Since that time, it has become well established that infections, such as toxoplasmosis, syphilis, and HIV may be a causative factor in psychosis,<sup>3,4</sup> and the number of types of infection associated with psychosis continues to expand to include influenza, Ebola, severe acute respiratory syndrome (SARS), Middle East respiratory syndrome, dengue, and Zika.<sup>5–9</sup> Population-wide incidence of psychosis during respiratory epidemics and pandemics has been estimated to be 60-fold higher than median baseline incidence of psychosis.<sup>6</sup> In a 6-month retrospective cohort evaluating psychiatric outcomes of 236,379 COVID-19 survivors, 1.4% developed a psychotic disorder. Interestingly, COVID-19–associated psychosis was more than 2-fold higher than influenza-associated psychosis and more than 1.6-fold higher for any respiratory

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Table 1. Case Reports of Psychosis Related to COVID-19

Case Report	Age/Sex	Past Psychiatric History	Delusions	AVTH	Disorganized	Antipsychotic
Alba et al, 2021 <sup>12</sup>	40/male	Negative	Positive	Visual	Positive	Aripiprazole 5 mg
Chacko et al, 2020 <sup>13</sup>	52/male	Negative	Positive	...	...	Emergency haloperidol 5 mg and lorazepam 2 mg x 1, olanzapine 10 mg (5 mg twice/d), 6 ECT treatments
Ferrando et al, 2020 <sup>14</sup> Case 1	20/male	Negative	Positive	Auditory	Positive	Quetiapine 25 mg
Ferrando et al, 2020 <sup>14</sup> Case 2	34/female	Panic disorder	Positive	...	Positive	Aripiprazole 5 mg
Ferrando et al, 2020 <sup>14</sup> case 3	33/male	Opioid use disorder	Positive	Auditory	...	Quetiapine 50 mg twice/d
Ignatova et al, 2021 <sup>15</sup>	43/male	Negative	Positive	...	Positive	Haloperidol, zuclopenthixol, promethazine, haloperidol 9 mg, olanzapine 10 mg
Kozato et al, 2021 <sup>16</sup>	"Middle aged"/male	Negative	Positive	Auditory, tactile	Positive	Risperidone 4 mg
Lanier et al, 2022 <sup>17</sup>	58/male	Anxiety, panic	...	Auditory	...	Haloperidol 2.5 mg, lorazepam as needed
Majadas et al, 2020 <sup>18</sup>	63/male	Negative	Positive	Auditory	Positive	Risperidone 6 mg
Mirza et al, 2020 <sup>19</sup>	53/male	Negative	...	Auditory, visual	Positive	Olanzapine 5 mg/d on 3 days
Parra et al, 2020 <sup>20</sup>	10 patients: mean age of 54 y/ not individually described	1 patient (schizoid)	10 patients	Auditory hallucinations: 4 patients Visual hallucinations: 1 patient	...	<ul style="list-style-type: none"> <li>Olanzapine, 7 of 10 patients, average dose of 15 mg</li> <li>Aripiprazole, 1 of 10 patients, average dose of 10 mg</li> <li>Risperidone, 5 of 10 patients, average dose of 2.2 mg</li> <li>Haloperidol, 3 of 10 patients, average dose of 2 mg</li> </ul>
Parker et al, 2021 <sup>21</sup>	57/male	Negative	Positive	Auditory, visual	Positive	Emergency: haloperidol 5 mg and lorazepam 2 mg x 2 Aripiprazole 20 mg, then cross-titration to risperidone 6 mg
Smith et al, 2020 <sup>22</sup>	36/female	Negative	Positive	...	Positive	Olanzapine 5 mg then cross-titration to risperidone 3 mg
Rentero et al, 2020 <sup>23</sup>	"A number of" patients with psychosis; all had delusions, some auditory hallucinations; antipsychotics used; resolution ≤ 2 weeks	...	...	...	...	...

Abbreviations: AVTH = auditory, visual, tactile hallucinations, COVID-19 = coronavirus disease 2019, ECT = electroconvulsive.

infection-associated psychosis.<sup>10</sup> This may be due to the extraordinary inflammatory and cytokine storm of COVID-19, which dysregulates neurotransmission.<sup>11</sup>

To date, there have been at least 14 case reports covering at least 23 cases of psychosis associated with COVID-19 (Table 1).<sup>12–23</sup> Importantly, no cases of COVID-associated psychosis published to date have required COVID-specific treatment for psychosis. This contrasts with other forms of psychosis secondary to a medical condition, wherein treating the underlying condition is often necessary for resolution of psychosis.<sup>3</sup> This may be because COVID is often a self-limiting virus, provided an individual survives the infection. Interestingly, antipsychotics, such as haloperidol, chlorpromazine, and the experimental 5-HT<sub>2A</sub> blocker cinanserin have demonstrated efficacy in treating SARS coronavirus in vitro and in vivo, and it may be possible that treatment with antipsychotics during COVID-associated psychosis also aids in the COVID resolution.<sup>24–26</sup>

The current case presents a patient with preexisting schizoaffective disorder who experienced acute worsening of psychosis temporally related to COVID-19 infection. Although it is possible that the presentation could have occurred during the natural course of his psychotic illness, the dramatic worsening of psychosis during his acute infection was notable. In particular, the patient's level of violence due to command auditory hallucinations has never occurred in the patient's 15-year history of schizoaffective disorder. The actionable lesson from this case is that COVID-19 may cause worsening of psychosis in patients with preexisting psychotic disorders and that the most likely treatment avenue remains dopamine-blocking agents.

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